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## NOTICE OF ALLOWANCE AND FEE(S) DUE

7590

04/30/2008

Stephen M Haracz Bryan Cave 1290 Avenue of the Americas New York, NY 10104 EXAMINER
SWOPE, SHERIDAN

PAPER NUMBER

ART UNIT

DATE MAILED: 04/30/2008

	APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/560,726 12/08/2005		12/08/2005	Renyuan Bai	K21788USWO	3759
	TITLE OF INITENTION, E	CEDDACK DEGICEANTE A	MENTAL CONTACTE IZINIA CIEC	(C038435/01953	

TITLE OF INVENTION: FEEDBACK-RESISTANT MEVALONATE KINASES

APPLN. TYPE	SMALL ENTITY	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	NO	\$1440	\$300	\$0	\$1740	07/30/2008

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE DOES NOT REFLECT A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE IN THIS APPLICATION. IF AN ISSUE FEE HAS PREVIOUSLY BEEN PAID IN THIS APPLICATION (AS SHOWN ABOVE), THE RETURN OF PART B OF THIS FORM WILL BE CONSIDERED A REQUEST TO REAPPLY THE PREVIOUSLY PAID ISSUE FEE TOWARD THE ISSUE FEE NOW DUE.

#### HOW TO REPLY TO THIS NOTICE:

I. Review the SMALL ENTITY status shown above.

If the SMALL ENTITY is shown as YES, verify your current SMALL ENTITY status:

A. If the status is the same, pay the TOTAL FEE(S) DUE shown above.

B. If the status above is to be removed, check box 5b on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and twice the amount of the ISSUE FEE shown above, or

If the SMALL ENTITY is shown as NO:

A. Pay TOTAL FEE(S) DUE shown above, or

B. If applicant claimed SMALL ENTITY status before, or is now claiming SMALL ENTITY status, check box 5a on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and 1/2 the ISSUE FEE shown above.

II. PART B - FEE(S) TRANSMITTAL, or its equivalent, must be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed and an extra copy of the form should be submitted. If an equivalent of Part B is filed, a request to reapply a previously paid issue fee must be clearly made, and delays in processing may occur due to the difficulty in recognizing the paper as an equivalent of Part B.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.

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### Complete and send this form, together with applicable fee(s), to: Mail Mail Stop ISSUE FEE

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INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required), Blocks 1 through 5 should be completed where

appropriate. All further correspondence including the Patent, advance orders and notification indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new maintenance fee notifications.  CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)				not maintenance fees will be mailed to the current correspondence address as correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.			
Stephen M Hai Bryan Cave 1290 Avenue of	the Americas	/2008		Cert	tificate (	of Mailing or Transn	nission deposited with the United class mail in an envelope above, or being facsimile te indicated below.
New York, NY	10104						(Depositor's name)
							(Signature)
							(Date)
APPLICATION NO.	FILING DATE		FIRST NAMED INVENT	OR	ATTOR	NEY DOCKET NO.	CONFIRMATION NO.
10/560,726 FITLE OF INVENTION	12/08/2005 I: FEEDBACK-RESISTA	ANT MEVALONATE K	Renyuan Bai INASES			21788USWO 038435/01953	3759
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nonprovisional	NO	\$1440	\$300	\$0		\$1740	07/30/2008
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SWOPE, S.		1652	435-194000	_			
Change of corresp Address form PTO/SI "Fee Address" ind PTO/SB/47; Rev 03-( Number is required. 3. ASSIGNEE NAME A PLEASE NOTE: Unl	ND RESIDENCE DATA less an assignee is identi h in 37 CFR 3.11. Comp	(I) the names of up or agents OR, altern (2) the name of a sin registered attorney of 2 registered patent a listed, no name will THE PATENT (print or data will appear on the	ngle firm (having as a or agent) and the name ttorneys or agents. If i be printed. type) patent. If an assigne an assignment.	members of upno name	r a 2to is 3	cument has been filed for	
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a. Applicant claim	tus (from status indicated as SMALL ENTITY statu d Publication Fee (if requestroords of the United Sta	ıs. See 37 CFR 1.27.	b. Applicant is no l	onger claiming SMAL	L ENT	TY status. See 37 CF.	
·				Date			
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This collection of inform in application. Confiden submitting the completed his form and/or suggesti	nation is required by 37 C tiality is governed by 35 d application form to the ions for reducing this bu	FR 1.311. The informatic U.S.C. 122 and 37 CFR USPTO. Time will vary rden, should be sent to th	on is required to obtain on 1.14. This collection is depending upon the infection Office Chief Information Office.	or retain a benefit by the estimated to take 12 r dividual case. Any co licer, U.S. Patent and	ne public ninutes mments Fradema	c which is to file (and to complete, including on the amount of tim ark Office, U.S. Depar	by the USPTO to process) g gathering, preparing, and he you require to complete rtment of Commerce, P.O.

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Stephen M Haracz			SWOPE, S	HERIDAN
Bryan Cave			ART UNIT	PAPER NUMBER
1290 Avenue of the New York, NY 101			1652 DATE MAILED: 04/30/200	8

## Determination of Patent Term Adjustment under 35 U.S.C. 154 (b)

(application filed on or after May 29, 2000)

The Patent Term Adjustment to date is 134 day(s). If the issue fee is paid on the date that is three months after the mailing date of this notice and the patent issues on the Tuesday before the date that is 28 weeks (six and a half months) after the mailing date of this notice, the Patent Term Adjustment will be 134 day(s).

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) WEB site (http://pair.uspto.gov).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 or (571)-272-4200.

	Application No.	Applicant(s)				
	10/560.726	BAI ET AL.				
Notice of Allowability	Examiner	Art Unit				
	SHERIDAN SWOPE	1652				
The MAILING DATE of this communication apperature All claims being allowable, PROSECUTION ON THE MERITS IS herewith (or previously mailed), a Notice of Allowance (PTOL-85) NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT R of the Office or upon petition by the applicant. See 37 CFR 1.313	(OR REMAINS) CLOSED in this appropriate communication IGHTS. This application is subject	pplication. If not included on will be mailed in due course. <b>THIS</b>				
1. This communication is responsive to <u>January 7, 2008</u> .						
2. ☑ The allowed claim(s) is/are <u>1-7,9 and 11-20</u> .						
<ul> <li>3.  Acknowledgment is made of a claim for foreign priority until a)   All   b)  Some*  c)  None  of the:</li> <li>1.  Certified copies of the priority documents have</li> <li>2.  Certified copies of the priority documents have</li> <li>3.  Copies of the certified copies of the priority do</li> </ul>	e been received. e been received in Application No. <sub>-</sub>					
International Bureau (PCT Rule 17.2(a)).						
* Certified copies not received:						
Applicant has THREE MONTHS FROM THE "MAILING DATE" noted below. Failure to timely comply will result in ABANDONN THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.  4.   A SUBSTITUTE OATH OR DECLARATION must be subm	MENT of this application.					
INFORMAL PATENT APPLICATION (PTO-152) which give						
5. CORRECTED DRAWINGS ( as "replacement sheets") must	st be submitted.					
(a) including changes required by the Notice of Draftspers	·	0-948) attached				
1)  hereto or 2)  to Paper No./Mail Date						
(b) ☐ including changes required by the attached Examiner'	s Amendment / Comment or in the	Office action of				
Identifying indicia such as the application number (see 37 CFR 1	Paper No./Mail Date  Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).					
6. DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.						
Attachment(s) 1. ☐ Notice of References Cited (PTO-892)	5. ☐ Notice of Informal	Patent Application				
<ol> <li>Notice of References Cited (PTO-092)</li> <li>D Notice of Draftperson's Patent Drawing Review (PTO-948)</li> </ol>	6. ☐ Interview Summar	• •				
3. ☐ Information Disclosure Statements (PTO/SB/08),	Paper No./Mail Da 7. ⊠ Examiner's Amend	ate				
Paper No./Mail Date  4. Examiner's Comment Regarding Requirement for Deposit		nent of Reasons for Allowance				
of Biological Material	<b>-</b> 9.					

#### DETAILED ACTION

Applicant's response, on January 7, 2008, to the Action on the Merits of this case mailed October 16, 2007, is acknowledged. It is acknowledged that Applicants have cancelled Claims 8 and 10 and amended Claims 1-4, 9, 11-14, 16, 19, and 20. Claims 1-7, 9, and 11-20 are pending. Claims 5-7, 17, and 18 were previously withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim. Claims 1-4, 9, 11-16, 19, and 20 are hereby reconsidered.

#### Examiner's Amendment

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to Applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

### Rejoinder

Restriction of Claims 5-7, 17, and 18 is withdrawn.

### **Claims**

For Claim 1, line 3, replace –wherein– with – wherein the non-modified mevalonate kinase is a naturally occurring fungal or bacterial mevalonate kinase,–.

For Claim 20, line 5, replace –inhibition; – with – inhibition, wherein the first mevalonate kinase is a naturally occurring fungal or bacterial mevalonate kinase; –.

Authorization for this examiner's amendment was given in a telephone interview with Charles Avigliano on March 24, 2008.

## Allowable Subject Matter

Claims 1-7, 9, and 11-20 are allowed.

The following is an examiner's statement of reasons for allowance:

All allowable claims, Claims 1-7, 9, and 11-20, are limited to an isolated modified mevalonate kinase protein derived from any naturally occurring fungal or bacterial mevalonate kinase, wherein the modified mevalonate kinase has at least 95% identity to SEQ ID NO: 1 and has a mutation at the residue corresponding to Ile<sup>17</sup> of SEQ ID NO: 1. The utility of said proteins as having mevalonate kinase activity is credible based on expression of variants of SEQ ID NO: 1 in heterologous host cells and analysis by an enzymatic assay (Table 1). Moreover, modified mevalonate kinases having a mutation at the residue corresponding to Ile<sup>17</sup> of SEQ ID NO: 1 have an unexpected and advantageous reduction in feedback inhibition (Table 1). Mevalonate kinases have real-world utility in the production of isoprenoid compounds such as ubiquinone-10, heme, dolichol, and cholesterol, as well as farnesyl and geranylgeranyl groups (Houten et al, 2000; IDS). Therefore, the encompassed modified mevalonate kinases have a specific and substantial, patentable utility.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan L. Swope whose telephone number is 571-272-0943. The examiner can normally be reached on M-F; 9:30-7 EST.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Nashed can be reached on 571-272-0934. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent

Application Information Retrieval (PAIR) system. Status information for published application

may be obtained from either Private PAIR or Public PAIR. Status information for unpublished

applications is available through Private PAIR only. For more information about the PAIR

system, see <a href="http://pair-direct.uspto.gov">http://pair-direct.uspto.gov</a>. Should you have questions on the access to the Private

PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/SHERIDAN SWOPE/

Primary Examiner, Art Unit 1652